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Effectiveness of Combined Spirulina (Arthrospira Platensis) And Red Dragon Fruit Peel (Hylocereus Polyrhizus) Infusion on LDL and HDL Levels In Hyperlipidemic Rats

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Abstract: Hyperlipidemia is a lipid-metabolism disorder that increases cardiovascular risk through elevated low-density lipoprotein and reduced high-density lipoprotein. Spirulina (Arthrospira platensis) and red dragon fruit peel (Hylocereus polyrhizus) contain bioactive compounds with potential lipid-modulating activity. This study analyzed the effectiveness of their combined infusion on low-density lipoprotein and high-density lipoprotein levels in hyperlipidemic male rats. A laboratory experimental design was applied to 25 male white rats aged 2-3 months and weighing 150-200 g. The rats were divided into five groups: hyperlipidemic control, simvastatin control, and three combined-infusion groups. Hyperlipidemia was induced using quail egg yolk for 24 days, followed by 14 days of intervention. Lipid levels were analyzed using normality, homogeneity, paired comparison, non-parametric, analysis of variance, and post-hoc tests. The combined infusion significantly reduced low-density lipoprotein levels in all treatment groups ($p < 0.05$). High-density lipoprotein levels increased after intervention but were not statistically significant ($p > 0.05$). The combined infusion improved lipid profile mainly through low-density lipoprotein reduction, while high-density lipoprotein improvement remained statistically non-significant.

Keyword: HDL, Hyperlipidemia, LDL, Red Dragon Fruit Peel, Spirulina

INTRODUCTION

Hyperlipidemia is a metabolic condition in which circulating lipid fractions exceed physiological needs and create an atherogenic environment. The disorder is commonly expressed through elevation of total cholesterol, triglycerides, or low-density lipoprotein cholesterol and may also involve decreased high-density lipoprotein cholesterol. In clinical and experimental contexts, the disorder is important because lipid disturbances are not only laboratory abnormalities but also biological drivers of vascular inflammation, oxidative modification, endothelial dysfunction, and progressive plaque formation. The burden of dyslipidemia therefore makes lipid control an essential component of cardiovascular prevention, especially when dietary fat intake, sedentary behavior, and other lifestyle factors continuously increase exposure to atherogenic particles (Ezeh & Ezeudemba, 2021; Ference et al., 2017; Mach et al., 2020)

Low-density lipoprotein is considered a major atherogenic lipoprotein because it carries cholesterol into peripheral tissues and can accumulate in the vascular wall when present in excess. Once retained in the intima, LDL particles may undergo oxidation and other modifications, triggering monocyte recruitment, macrophage uptake, foam-cell formation, and plaque development. The causal role of LDL in atherosclerotic cardiovascular disease has been supported by genetic, epidemiological, and clinical trial evidence, and LDL reduction remains a major target of lipid-lowering management. In contrast, high-density lipoprotein participates in reverse cholesterol transport and has antioxidant, anti-inflammatory, and endothelial-protective functions, although HDL functionality is more complex than a simple increase in concentration (Ference et al., 2017; Rader & Hovingh, 2014; von Eckardstein et al., 2023).

Conventional management of dyslipidemia relies strongly on statins and other pharmacological agents. Statins reduce hepatic cholesterol synthesis and increase LDL receptor activity, thereby lowering circulating LDL. Nevertheless, complementary approaches using foods, algae, and plant-derived materials remain relevant because lipid disorders are closely connected to dietary exposure and oxidative stress. Functional ingredients are not intended to replace evidence-based medication in high-risk patients, but they can provide experimental insight into the biological modulation of lipid metabolism. Animal models are useful at this stage because they permit controlled induction of hyperlipidemia, standardized dosing, and repeated biochemical measurements before human trials are considered (Friedewald et al., 1972; Mach et al., 2020)

Spirulina, taxonomically known as *Arthrospira platensis*, is a cyanobacterium widely investigated as a nutritional supplement. Its bioactive profile includes phycocyanin, carotenoids, phenolic compounds, peptides, minerals, and unsaturated fatty acids. Reviews and meta-analyses have reported that spirulina supplementation may improve lipid parameters, including total cholesterol, LDL, triglycerides, and HDL, although effects vary according to dose, population, duration, baseline lipid status, and product form. Experimental studies in high-fat-diet animals have also shown that *Arthrospira platensis* can reduce cardiometabolic risk markers and mitigate hypercholesterolemia, supporting its potential as a functional ingredient for lipid profile improvement (Cacciola, De Cicco, Milanovic, et al., 2024; Deng & Chow, 2010; Huang et al., 2018; Serban et al., 2016).

Red dragon fruit peel, obtained from *Hylocereus polyrhizus*, is another material of interest because it is often discarded despite containing antioxidant constituents. The peel has been reported to contain phenolics, flavonoids, betalain pigments, fiber, and other compounds that may influence lipid metabolism. Studies comparing dragon fruit pulp and peel have shown that peel fractions may have substantial antioxidant activity, and experimental studies have reported lipid-profile improvement after red dragon fruit peel administration in hyperlipidemic animals. Such findings are relevant because the peel is an agricultural by-product that may be valorized into a health-related preparation rather than remaining as food waste (Hermawan, 2024; Nurliyana et al., 2010; Panjaitan & Amelia, 2022; Putriningtyas et al., 2020; Wybraniec & Mizrahi, 2002)

The combination of spirulina and red dragon fruit peel may offer complementary effects. Spirulina contributes phycocyanin and other nutrient-dense bioactive compounds, whereas dragon fruit peel provides polyphenols, antioxidant pigments, and dietary fiber components. These compounds may support lipid profile improvement by reducing lipid oxidation, limiting cholesterol absorption, and helping maintain the balance between LDL and HDL. The antioxidant activity of both materials is also relevant because oxidative stress can worsen lipid abnormalities and promote LDL oxidation in hyperlipidemic conditions. In addition, fiber and polyphenol components from dragon fruit peel may support cholesterol elimination, while spirulina may contribute to better lipid regulation through its bioactive protein and pigment compounds. However, combination data are still limited because previous studies mostly evaluated spirulina or dragon fruit peel separately, leaving a research gap regarding their combined effect in a hyperlipidemic animal model.

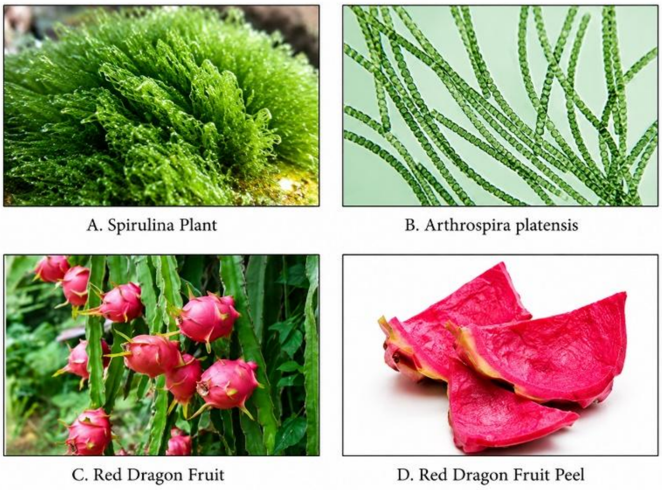

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Figure 1. Spirulina and Red Dragon Fruit Peel Materials

Based on this gap, the present study examined the effectiveness of combined spirulina and red dragon fruit peel infusion on LDL and HDL levels in male rats with experimentally induced hyperlipidemia. The research question was whether the combined infusion could significantly reduce LDL and increase HDL after high-fat induction. The results are expected to contribute to experimental health science by providing early evidence on a functional infusion formula based on algae and fruit-peel by-products.

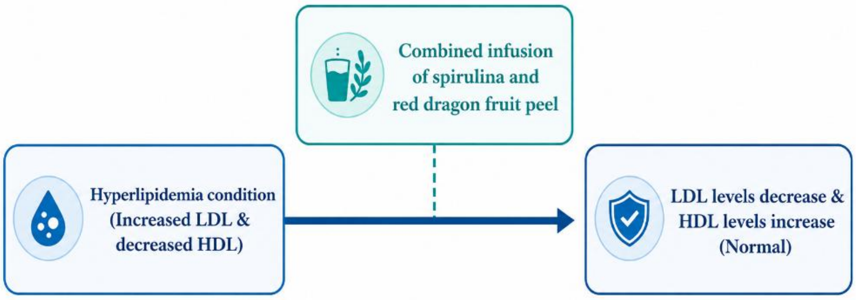

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Figure 2. Conceptual framework of the combined infusion and lipid-profile response

METHOD

This study was an experimental laboratory study using male white rats as a hyperlipidemic animal model. The use of an animal model was selected because lipid metabolism changes, particularly LDL and HDL responses, can be observed under controlled dietary induction and treatment conditions. The research employed a comparison group design consisting of five experimental groups, with each group containing five rats. This design allowed comparison between the hyperlipidemic control group, the standard drug group, and three treatment groups receiving different dose compositions of the combined spirulina and red dragon fruit peel infusion. The experimental animals were male white rats aged approximately 2-3 months, with body weight within the healthy adult range commonly used in laboratory experiments. Male rats were selected to minimize hormonal variation that may influence lipid metabolism. The inclusion criteria were physically healthy rats, active movement, normal feeding behavior, and absence of visible anatomical defects or signs of illness. Animals that showed severe weakness, abnormal behavior, injury, or death during the experimental process were excluded from the study. The number of animals was determined using Federer's formula for experimental group designs, resulting in a minimum of five animals in each group. Therefore, the total number of rats used in this study was 25.

The study was conducted at the Animal Laboratory of the Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta. Before treatment, all rats underwent an adaptation period to allow them to adjust to the laboratory environment, cage conditions, feeding pattern, and handling procedures. This adaptation stage was important to reduce stress-related physiological changes that could affect the lipid profile. After the adaptation period, the rats were induced into a hyperlipidemic condition using quail egg yolk as a high-fat dietary source for 24 days. Quail egg yolk was used because it contains high lipid and cholesterol components that can increase LDL levels and disturb lipid balance in experimental animals. After the induction period, treatment was administered for 14 days according to group allocation. Group I served as the hyperlipidemia control group and did not receive an active lipid-lowering agent. This group was used to observe lipid profile changes in hyperlipidemic rats without therapeutic intervention. Group II served as the positive control group and received simvastatin as the standard lipid-lowering therapy. The inclusion of the simvastatin group provided a comparison between the natural infusion treatment and a commonly used pharmacological agent. Groups III, IV, and V received the combined infusion of spirulina and red dragon fruit peel at different dose compositions, as presented in Table 1. These three groups were designed to evaluate whether dose variation influenced the ability of the combined infusion to reduce LDL levels and improve HDL levels.

During the experimental period, the rats were monitored regularly to observe general condition, food intake behavior, activity, and body weight changes. Body weight measurement was included as a supporting observation because changes in body weight may reflect metabolic adaptation during high-fat diet induction and treatment. Blood samples were collected at predetermined observation points to measure LDL and HDL levels. The comparison of lipid profile values before induction, after induction, and after treatment was used to determine the effect of the combined spirulina and red dragon fruit peel infusion on hyperlipidemic conditions. Through this design, the study aimed to evaluate the potential of the combined infusion as a natural antihyperlipidemic agent

Table 1. Treatment groups and intervention composition

Group	Model or treatment	Composition
I	Hyperlipidemia control	High-fat induction without active lipid-lowering intervention
II	Positive control	High-fat induction followed by simvastatin
III	Combined infusion 1	Spirulina 0.3 g + red dragon fruit peel 4.3 g
IV	Combined infusion 2	Spirulina 0.4 g + red dragon fruit peel 4.3 g
V	Combined infusion 3	Spirulina 0.5 g + red dragon fruit peel 8.6 g

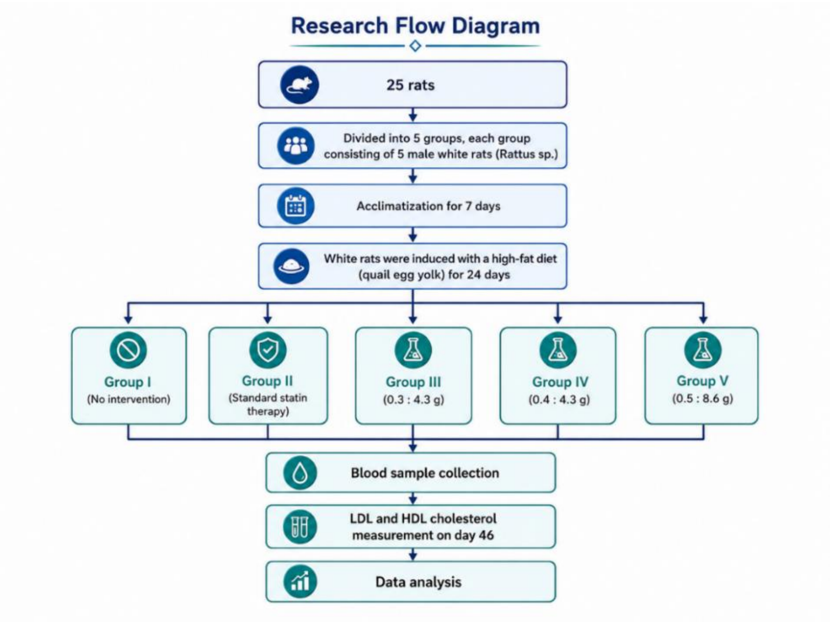
Source: Research data

The independent variable in this study was the dose composition of the combined infusion of *Spirulina* (*Arthrospira platensis*) and red dragon fruit peel (*Hylocereus polyrhizus*). The treatment doses were arranged in different formulations to observe whether variations in the proportion of both natural materials produced different effects on lipid profile improvement. The dependent variables were serum Low Density Lipoprotein (LDL) and High Density Lipoprotein (HDL) levels, measured in mg/dL as the main indicators of lipid metabolism response in hyperlipidemic rats. In addition, body weight was recorded as a supporting parameter to monitor the general physiological condition of the animals during the experimental period and to ensure that changes in lipid profile were not interpreted separately from the animals' overall metabolic status.

The combined infusion was prepared using dried spirulina and dried red dragon fruit peel according to the predetermined formulation. The dried materials were processed with water using the infusion method, allowing the water-soluble bioactive compounds to be extracted before administration to the experimental animals. Lipid profile measurements were conducted at three observation points, namely at baseline, after the induction of hyperlipidemia, and after the intervention period. Baseline measurement was used to describe the initial condition of the animals before high-fat diet induction. The second measurement was intended to confirm the development of hyperlipidemic conditions after induction using a high-fat diet. The final measurement was performed to evaluate the therapeutic response after administration of the combined infusion or standard treatment.

Data analysis was carried out by comparing LDL and HDL values across different measurement times and treatment groups. Before selecting the statistical test, the distribution of data was assessed using the Shapiro-Wilk test, while homogeneity of variance was evaluated to determine whether the data met the assumptions for parametric analysis. When the data were normally distributed and homogeneous, parametric tests were applied, including paired comparison tests, one-way analysis of variance, and post-hoc least significant difference testing. When the data did not meet the assumptions of normality or homogeneity, non-parametric tests were used, including the Wilcoxon signed-rank test, Friedman test, and Mann-Whitney test. The level of statistical significance was set at $p < 0.05$.

The interpretation of findings was not based solely on statistical significance, but also considered the biological direction and magnitude of changes in LDL, HDL, and the LDL/HDL ratio. A decrease in LDL levels was interpreted as an improvement in atherogenic lipid profile, while an increase in HDL levels was considered a favorable response related to reverse cholesterol transport. The LDL/HDL ratio was also examined because it provides a more comprehensive picture of lipid balance than LDL or HDL alone. Therefore, the effectiveness of the combined infusion was evaluated by integrating statistical results with biological relevance, particularly in determining whether the treatment showed potential as a natural antihyperlipidemic agent.



Source: Research documentation

Figure 3. Research flow diagram from animal grouping to lipid analysis

RESULT AND DISCUSSION

Body weight was monitored to determine whether the intervention produced marked changes in general physiological condition. The mean body weight before and after infusion showed only small shifts. Group II and groups III and IV tended to show lower or stable body weight after treatment, whereas groups I and V showed slight increases. These changes should be interpreted cautiously because body weight in short-term animal experiments is influenced by feed intake, stress adaptation, cage activity, hydration, and individual metabolic response. In the context of this study, body weight served as a supporting parameter rather than the main outcome.

Table 2. Mean body weight before and after infusion

Group	Before infusion day 31 (g)	After infusion day 45 (g)	Change
I	181.20 ± 49.30	185.00 ± 25.87	-3.80 ± 53.65
II	195.80 ± 15.27	186.00 ± 18.41	9.80 ± 7.69
III	173.40 ± 21.03	169.40 ± 21.22	4.00 ± 8.22
IV	177.00 ± 24.63	176.40 ± 25.64	0.60 ± 10.31
V	185.80 ± 35.41	188.80 ± 34.54	-3.00 ± 22.83

Source: Research data

The body-weight data also help to contextualize the interpretation of lipid results. A reduction in LDL after treatment could be partly influenced by altered intake or body-weight change, but the limited body-weight shift suggests that lipid modulation was not merely a consequence of large weight loss. The short duration of treatment may also explain why body weight was relatively stable, while biochemical parameters were more responsive. Similar short-term experimental studies often detect serum lipid changes before large changes in body mass become apparent.

LDL values increased after the high-fat induction phase in all groups. This response shows that the quail egg yolk induction was sufficient to produce a hyperlipidemic pattern. The highest mean LDL after induction was observed in the hyperlipidemia control group, while all intervention groups also demonstrated marked increases compared with baseline. The LDL elevation is consistent with the biological role of dietary lipid exposure in increasing circulating atherogenic lipoproteins. LDL is a priority target because excessive LDL contributes to atherosclerotic plaque formation and is strongly linked to cardiovascular risk (Ference et al., 2017; Mach et al., 2020)

Table 3. LDL levels during the experiment

Group	Baseline day 7	Hyperlipidemic day 31	Post-infusion day 45	LDL reduction day 31-45
I	108.61 ± 6.88	332.97 ± 76.31	163.69 ± 16.65	160.34 ± 69.82
II	117.73 ± 25.22	314.03 ± 67.63	152.47 ± 15.51	161.57 ± 75.13
III	106.52 ± 16.11	261.95 ± 45.15	170.38 ± 21.03	91.57 ± 25.11
IV	147.24 ± 32.53	207.82 ± 16.95	179.81 ± 14.88	28.00 ± 25.57
V	127.03 ± 22.72	250.54 ± 23.01	175.41 ± 19.39	75.14 ± 40.85

Source: Research data

showed a reduction similar in magnitude to the hyperlipidemia control group, whereas the combined infusion groups showed varied reductions. Group III showed the largest LDL reduction among the infusion groups, followed by group V and group IV. The statistical analysis showed significant LDL reduction, indicating that the intervention period was associated with a measurable improvement in atherogenic lipid burden. Although the magnitude of reduction differed among groups, the direction of change was consistent with the study objective.

The strongest LDL-lowering response among the infusion groups occurred in group III, which received spirulina 0.3 g and red dragon fruit peel 4.3 g. This result suggests that the lowest combined dose in this study was sufficient to influence LDL metabolism. The response was not strictly dose-dependent because increasing the amount of spirulina and peel did not produce a proportionally greater LDL reduction. Such a pattern is possible in herbal and functional-food studies because bioactive compounds may have threshold effects, matrix interactions, absorption limitations, or non-linear pharmacodynamic responses. Therefore, a higher dose should not automatically be interpreted as more effective

The LDL-lowering activity of spirulina may be explained through several mechanisms. Spirulina contains phycocyanin and other antioxidant constituents that can reduce oxidative stress and inflammation, both of which are closely linked to lipid metabolism. Reviews and clinical meta-analyses have reported hypolipidemic effects of spirulina supplementation, including reductions in total cholesterol and LDL. Experimental evidence in high-fat-diet rats also indicates that *Arthrospira platensis* may reduce cardiometabolic risk factors and improve serum lipid profiles. These mechanisms plausibly support the LDL reduction observed in the present study (Cacciola, De Cicco, Milanovic, et al., 2024; Deng & Chow, 2010; Huang et al., 2018; Serban et al., 2016).

Dragon fruit peel may strengthen this effect through its phenolic and pigment components. Red dragon fruit peel has antioxidant activity and contains betalain-related pigments, phenolics, and fiber that may influence lipid absorption and lipid oxidation. Experimental studies on *Hylocereus polyrhizus* peel have reported improvements in blood lipid levels in hyperlipidemic animals, including LDL reduction and HDL improvement. These findings support the biological plausibility that the peel component in the infusion contributed to the lipid-modulating effect, especially when combined with spirulina (Hernawati & others, 2018; Nurliyana et al., 2010; Panjaitan & Amelia, 2022; Putriningtyas et al., 2020; Wybraniec & Mizrahi, 2002).

The combined formulation may also work through additive antioxidant effects. Oxidative modification of LDL is a key event in atherogenesis because oxidized LDL is more readily taken up by macrophages and promotes foam-cell formation. Antioxidant compounds in spirulina and red dragon fruit peel may reduce oxidative stress and protect lipid particles from modification. Although the present study measured LDL concentration rather than oxidized LDL, a lower LDL value after treatment can still be interpreted as an important improvement in lipid profile. Future studies should include oxidative stress markers to clarify whether antioxidant mechanisms directly mediate the lipid changes.

Table 4. Statistical comparison of LDL changes

Comparison	Test indication	p value	Interpretation
Baseline vs hyperlipidemic phase	Induction effect	0.000*	Significant LDL increase after high-fat induction
Baseline vs post-intervention	Overall change	0.001*	Significant difference from baseline
Hyperlipidemic phase vs post-intervention	Treatment response	0.268	Between-time comparison was not significant in pooled interpretation
Post-intervention between groups	Post-hoc pattern	Group III, IV, and V differed from controls in selected comparisons	Infusion groups showed variable LDL response

Source: Research data, processed from statistical output

HDL values showed a different pattern from LDL. HDL decreased after high-fat induction and increased after treatment in all groups, but the increase was not statistically significant. This finding indicates that the combined infusion had a stronger and more consistent effect on LDL than on HDL. HDL concentration may require a longer intervention period, different dose composition, or measurement of HDL functionality rather than concentration alone. HDL biology is complex because the protective role of HDL depends not only on the amount of HDL cholesterol but also on cholesterol efflux capacity, antioxidant function, anti-inflammatory activity, and interactions with enzymes and apolipoproteins (Rader & Hovingh, 2014; von Eckardstein et al., 2023).

Table 5. HDL levels during the experiment

Group	Baseline day 7	Hyperlipidemic day 31	Post-infusion day 45	HDL increase day 31-45
I	108.61 ± 6.88	-29.35 ± 16.34	50.98 ± 13.11	21.69 ± 25.70
II	117.73 ± 25.22	-35.52 ± 49.51	48.65 ± 12.49	13.13 ± 56.77
III	106.52 ± 16.11	-35.15 ± 25.17	56.27 ± 23.67	21.12 ± 32.14
IV	147.24 ± 32.53	-36.76 ± 21.35	37.65 ± 14.25	8.98 ± 32.00
V	127.03 ± 22.72	-23.82 ± 30.64	66.21 ± 46.63	42.39 ± 66.22

Source: Research data

The highest HDL increase was observed in group V, which received spirulina 0.5 g and red dragon fruit peel 8.6 g. Although this increase was not statistically significant, it may be biologically meaningful because group V also showed the lowest LDL/HDL ratio after intervention. The wide standard deviation in HDL change indicates considerable individual variation among animals. With only five animals per group, variability can reduce statistical power and make it difficult to detect significant HDL changes. This limitation is common in small experimental animal studies and suggests that larger sample sizes may be needed for HDL-specific outcomes.

The non-significant HDL result does not necessarily mean that the infusion lacks biological activity. HDL concentration often changes more slowly than LDL because HDL metabolism depends on apoA-I production, cholesterol efflux from peripheral tissues, lecithin cholesterol acyltransferase activity, hepatic uptake, and remodeling by transfer proteins. Polyphenols and anthocyanins have been associated with improvements in lipid profiles, including HDL in some settings, but their effects are influenced by baseline metabolic status and treatment duration. Evidence from anthocyanin studies supports the possibility of HDL modulation, but the magnitude and consistency are not uniform across studies (Jang et al., 2023; Qin et al., 2009)

The data also show that HDL response differed across infusion compositions. Group III had a moderate HDL increase, group IV had the smallest increase, and group V had the largest increase. This pattern differs from LDL, where group III showed the greatest reduction. The difference suggests that LDL and HDL may respond to the combined infusion through partially distinct mechanisms. LDL reduction may be more related to inhibition of lipid absorption, antioxidant protection, or hepatic lipid handling, whereas HDL increase may require mechanisms linked to reverse cholesterol transport and apolipoprotein regulation.

The positive control group did not show the greatest increase in HDL levels because simvastatin primarily acts by inhibiting HMG-CoA reductase, thereby reducing hepatic cholesterol synthesis and producing a stronger effect on LDL reduction than on HDL elevation. In this context, the infusion demonstrated a potential comparative value in supporting lipid-balance modulation, particularly through its possible contribution to improving HDL levels. However, this finding should be interpreted cautiously because the observed increase in HDL was not statistically conclusive. Therefore, further studies with a larger sample size, longer treatment duration, and additional lipid parameters are needed to confirm the potential effect of the infusion on HDL improvement.

Table 6. Statistical comparison of HDL changes

Comparison	Test indication	p value	Interpretation
Baseline vs hyperlipidemic phase	Induction effect	0.000*	Significant HDL change after induction
Baseline vs post-intervention	Overall change	0.001*	Significant difference from baseline
Hyperlipidemic phase vs post-intervention	Treatment response	0.268	HDL increase after treatment was not statistically significant
Post-intervention between groups	Mann-Whitney pattern	$p > 0.05$ in pairwise comparisons	No significant between-group HDL difference

Source: Research data, processed from statistical output

The statistical comparison in Table 6 indicates that HDL levels changed significantly between baseline and the hyperlipidemic phase, showing that the high-fat diet induction affected HDL concentration. A significant difference was also found between baseline and post-intervention, suggesting an overall change in HDL levels after the complete observation period. However, the comparison between the hyperlipidemic phase and post-intervention showed no statistically significant improvement. This finding indicates that although HDL levels tended to increase after treatment, the increase was not strong enough to be considered statistically significant. The post-intervention comparison between groups also showed no significant difference, suggesting that the HDL response among the treatment groups was relatively similar. The overall pattern of LDL and HDL changes during the observation period is illustrated in Figure 4.

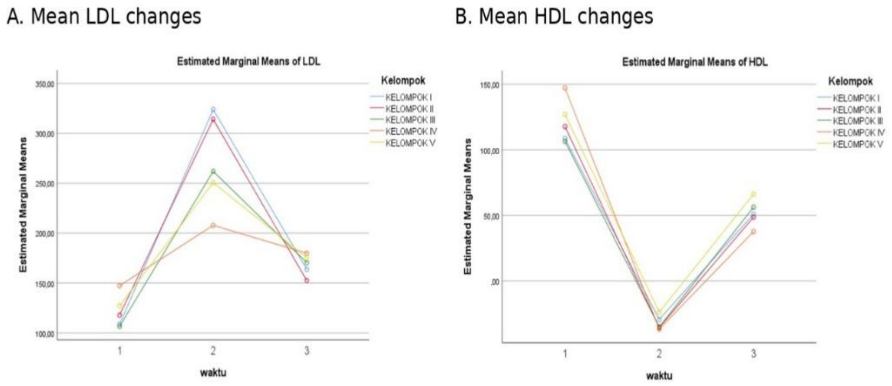


Figure 4. Mean LDL and HDL changes across the observation period

Source: Research documentation

The LDL/HDL ratio was calculated as an additional index of lipid balance. This ratio is useful because LDL and HDL have opposing roles in lipid transport and cardiovascular risk interpretation. A lower ratio indicates a more favorable relationship between atherogenic and protective lipoprotein fractions. In this study, group V had the lowest ratio after intervention, followed by group III, group II, group I, and group IV. This pattern suggests that group V showed the most favorable lipid balance after treatment, particularly because LDL reduction was followed by a relatively better HDL profile. The ratio provides a more integrated interpretation than LDL or HDL alone because it considers whether LDL reduction is accompanied by sufficient HDL concentration. Therefore, the LDL/HDL ratio strengthens the interpretation that the combined infusion may contribute to lipid profile improvement in hyperlipidemic rats.

Table 7. LDL/HDL ratio after intervention

Group	LDL (mg/dL)	HDL (mg/dL)	LDL/HDL ratio	Interpretation
I	163.69	50.98	3.21	Moderate
II	152.47	48.65	3.13	Moderate
III	170.38	56.27	3.03	Moderate
IV	179.81	37.65	4.78	High
V	175.41	66.21	2.65	Low

Source: Research data

Group V had a post-intervention LDL value close to the other infusion groups. In contrast, group IV had the highest ratio because its HDL value remained comparatively low despite a reduction in LDL. This ratio-based interpretation helps explain why the highest dose combination may still be relevant even though group III had the largest LDL reduction. If the objective is limited to LDL lowering, group III appears most promising. If the objective is overall LDL-HDL balance, group V deserves attention.

The findings show that the combined infusion should be discussed as a lipid-profile modulator rather than a single-target HDL enhancer. The significant LDL reduction is the strongest outcome, while HDL improvement remains suggestive but inconclusive. This interpretation is important for avoiding overstatement. The result supports the potential of spirulina and red dragon fruit peel infusion as an experimental complementary intervention, but it does not justify a clinical claim for human dyslipidemia management without further studies.

The results are consistent with previous literature showing lipid-modulating effects of the two ingredients separately. Spirulina supplementation has been associated with lower LDL and improved lipid profile in reviews and experimental studies, while red dragon fruit peel has been reported to improve lipid parameters in hyperlipidemic animal models. The present study extends this body of evidence by testing a combined infusion preparation. The combination approach is relevant because food-based bioactives are often consumed as mixtures rather than isolated compounds (Hernawati & others, 2018; Huang et al., 2018; Panjaitan & Amelia, 2022; Serban et al., 2016)

Overall, the discussion answers the research problem by showing that the combined infusion affected LDL significantly and improved HDL directionally but not significantly. The evidence is strongest for LDL reduction. The difference between LDL and HDL response emphasizes the need for cautious interpretation and more comprehensive mechanistic testing. The most appropriate conclusion is that the combined infusion improved lipid profile in hyperlipidemic rats primarily through LDL reduction, with the best ratio balance observed in group V.

Taken together, the figures and tables indicate that the combined infusion produced a more consistent and clearer response in LDL reduction than in HDL improvement. This pattern suggests that the infusion may have a stronger effect on lipid-lowering activity, particularly in relation to LDL modulation, while its influence on HDL remains less definitive. However, the results should still be interpreted as preliminary experimental evidence because the sample size was limited, the treatment duration was relatively short, and several important functional markers were not assessed. Parameters such as oxidized LDL, apolipoproteins, hepatic enzymes, inflammatory markers, and antioxidant capacity could provide a more comprehensive explanation of the possible mechanisms underlying the observed lipid changes. Therefore, future studies should standardize the phytochemical content of the infusion, evaluate dose-response relationships, and test longer intervention durations before broader health claims are made. These additional investigations are necessary to confirm whether the combined infusion has a sustained and clinically meaningful role in lipid-balance modulation.

Mechanistic Interpretation of The Infusion

The graphical presentation added to the manuscript clarifies that the experimental response occurred in two stages. The first stage was the elevation of LDL after high-fat induction, which confirms that the quail egg yolk model successfully produced an atherogenic pattern. The second stage was the decline of LDL after intervention, which occurred in the simvastatin group and in the three combined-infusion groups. This pattern supports the interpretation that the infusion had a measurable lipid-modulating effect rather than merely reflecting random fluctuation in lipid values.

The most plausible mechanism is not a single pharmacological pathway, but a combination of antioxidant, intestinal, and hepatic effects. Spirulina provides phycocyanin, carotenoids, and other antioxidant compounds that may reduce oxidative stress and inflammatory signaling. Red dragon fruit peel provides phenolic compounds, pigments, and fiber fractions that may reduce lipid absorption and support antioxidant protection. Previous literature has discussed hypolipidemic, antioxidant, and anti-inflammatory activity of spirulina, while dragon fruit peel has been reported as a source of antioxidant constituents (Deng & Chow, 2010; Nurliyana et al., 2010)

The decrease in LDL is also compatible with the biological role of LDL as the main carrier of cholesterol to peripheral tissues. When dietary lipid intake increases, the liver packages lipid into very-low-density lipoprotein, which can be converted into LDL in circulation. Any intervention that reduces intestinal lipid entry, increases hepatic LDL receptor activity, improves bile-acid excretion, or protects lipoproteins from oxidative modification may reduce circulating LDL. Because LDL is a central causal factor in atherosclerotic cardiovascular disease, the significant reduction observed in this animal model is an important preliminary result (Ference et al., 2017; Mach et al., 2020).

The HDL response requires more cautious interpretation. HDL concentration increased after treatment, but the statistical test did not show significance. This does not necessarily mean that HDL biology was unaffected. HDL metabolism depends on apolipoprotein A-I synthesis, cholesterol efflux, lecithin cholesterol acyltransferase activity, and particle remodeling. These processes may need a longer intervention period than LDL reduction. In addition, HDL function may be more relevant than HDL concentration alone, because dysfunctional HDL can lose protective capacity in chronic inflammatory or metabolic conditions (Rader & Hovingh, 2014; von Eckardstein et al., 2023)

The difference between LDL and HDL outcomes is therefore reasonable. LDL can decrease within a relatively short period when lipid intake or hepatic clearance changes, whereas HDL may require more stable remodeling of lipid transport and apolipoprotein metabolism. This explains why the intervention produced a significant LDL reduction but only a directional HDL increase. Future research should measure total cholesterol, triglycerides, oxidized LDL, apolipoprotein B, apolipoprotein A-I, and cholesterol efflux capacity to clarify whether the combined infusion affects lipid quantity, lipoprotein quality, or both.

Dose Response And Group Comparison

The group comparison also provides important information. Group III showed the most notable LDL-lowering response among the infusion groups, even though it did not contain the highest amount of spirulina or red dragon fruit peel. This finding suggests a non-linear dose response. In preparations derived from natural materials, higher dose does not always produce stronger biological effect because absorption, solubility, palatability, and interaction among compounds can influence bioavailability. Thus, the lowest combined dose in this study may have achieved a more favorable balance for LDL reduction.

Group V should not be ignored because it showed the most favorable LDL/HDL ratio. A ratio-based interpretation is useful because LDL and HDL have opposing roles in lipid transport. Group V did not provide the strongest LDL decline, but its HDL level after intervention was relatively higher than the other infusion groups. This explains why the ratio was better. Therefore, the recommended direction for future dose optimization depends on the target: group III is more promising for LDL reduction, while group V is more promising for overall lipid balance.

The absence of a simple dose-response pattern also shows why the combined infusion should not yet be translated into a fixed clinical recommendation. The study was conducted in a limited animal model and did not evaluate long-term safety, repeated-dose toxicity, or active-compound standardization. Before product development, the formulation should be tested across more dose combinations, longer treatment periods, and a normal control group. Such refinements would determine whether the observed effect is reproducible and whether the dose-response pattern remains stable.

Comparison With Previous Research

The present result is consistent with previous research on spirulina. Meta-analytic evidence and experimental studies have reported that spirulina supplementation may reduce total cholesterol and LDL, and in some conditions may improve HDL. Recent animal studies also show that *Arthrospira platensis* can reduce cardiometabolic risk factors in high-fat-diet models. These findings strengthen the interpretation that the spirulina fraction contributed to the LDL reduction observed in this study (Cacciola, De Cicco, Milanović, et al., 2024; Huang et al., 2018; Serban et al., 2016)

The present result is also aligned with studies on red dragon fruit peel. Previous experimental research reported that *Hylocereus polyrhizus* peel improved blood lipid levels in hyperlipidemic animals, while other studies described antihypercholesterolemic activity of red dragon fruit peel preparations. These findings support the use of the peel as a functional material rather than as agricultural waste. The current study extends that evidence by combining the peel with spirulina in an infusion preparation (Hernawati & others, 2018; Panjaitan & Amelia, 2022; Putriningtyas et al., 2020)

The pigment and polyphenol content of dragon fruit peel may partly explain its contribution. Anthocyanins and related polyphenolic compounds have been associated with improvements in serum LDL and HDL in dyslipidemic subjects and in systematic reviews. Although dragon fruit peel pigments are not identical to all anthocyanin preparations, the comparison supports the idea that plant pigments and polyphenols may influence lipid metabolism through antioxidant and regulatory pathways (Jang et al., 2023; Qin et al., 2009).

Scientific And Practical Implications

The scientific implication of this study is that a combined natural infusion can be positioned as a candidate for further lipid-profile research. The findings do not prove clinical efficacy in humans, but they provide a structured experimental basis for deeper study. The most defensible statement is that the infusion improved the lipid profile of hyperlipidemic rats, primarily through significant LDL reduction. Any broader health claim should wait for standardized animal replication, toxicity testing, and human studies.

The practical implication is related to the use of accessible biological materials. Spirulina is already recognized as a nutrient-rich supplement, while red dragon fruit peel is frequently discarded. Combining these two materials may support waste valorization and functional ingredient development. However, product development must include phytochemical standardization, microbial safety testing, stability testing, sensory evaluation, and dosage safety. Without these steps, a promising experimental preparation cannot yet be considered a safe public-health product.

Methodologically, the study has several limitations that should be acknowledged. The sample size was small, the intervention lasted only 14 days, and the amount of high-fat material consumed by each animal was not strictly controlled, so individual variation in quail egg yolk intake may have influenced the degree of hyperlipidemia and the response after treatment. The induction phase was also extended from the initially planned 14 days to 24 days to establish a hyperlipidemic condition. In addition, the combined infusion dose appeared more effective for reducing LDL than for increasing HDL, indicating that the tested dose compositions were not yet optimal for HDL-specific improvement. Future experiments should use larger groups, controlled intake recording, longer observation periods, and additional dose combinations to strengthen reproducibility.

The figures support the interpretation by linking the research materials, conceptual framework, experimental flow, and lipid trends. The visual presentation shows that LDL and HDL changed in different patterns, reinforcing that the strongest evidence from this experiment is LDL reduction, while HDL improvement remains descriptive and statistically inconclusive.

Future Analytical Development

Future analytical work should also compare the infusion with other preparation forms. Infusion is practical and close to household use, but water extraction may not collect all lipid-soluble antioxidants from spirulina and red dragon fruit peel. Ethanol extract, aqueous extract, powder suspension, and fermented preparations may produce different concentrations of phycocyanin, phenolics, betalains, and fiber-related compounds. Comparing these forms would help determine whether the lipid effect is caused mainly by water-soluble compounds or by the whole matrix of the materials.

Standardization is especially important because natural materials vary according to cultivation, harvest time, drying process, storage, and extraction temperature. Two infusions with the same gram composition may have different bioactive strength if the raw material differs. Therefore, future studies should report total phenolic content, flavonoid content, pigment concentration, antioxidant capacity, and microbial quality before administration. This would make the results more reproducible and would help connect the administered dose with the actual bioactive exposure received by the animals.

Another useful direction is histopathological evaluation. Measuring serum LDL and HDL provides biochemical evidence, but liver and vascular tissue observations would show whether lipid improvement is accompanied by organ protection. Liver histology could identify steatosis, inflammatory cell infiltration, or hepatocyte damage after high-fat induction and treatment. Vascular tissue observation could clarify whether the decrease in LDL is related to lower atherogenic burden. These additional data would strengthen the biological explanation of the combined infusion.

Safety evaluation should be developed together with efficacy evaluation. Although both materials are food-related, a concentrated combined infusion may have different effects from ordinary dietary exposure. Liver enzymes, kidney-function markers, hematological parameters, and behavioral observations should be monitored in longer studies. Such safety data are essential before the formulation is discussed as a functional product. In this manuscript, the finding should therefore be understood as experimental evidence, not as a recommendation for unsupervised human consumption.

CONCLUSION

The combined infusion of spirulina (*Arthrospira platensis*) and red dragon fruit peel (*Hylocereus polyrhizus*) improved the lipid profile of hyperlipidemic male rats, mainly through significant reduction of LDL levels. Among the infusion groups, the greatest LDL reduction was observed in group III, which received spirulina 0.3 g and red dragon fruit peel 4.3 g. HDL levels increased after treatment, with the highest increase in group V, but the change was not statistically significant. The LDL/HDL ratio showed the most favorable balance in group V, indicating that a higher peel-containing formulation may support overall lipid balance even when LDL reduction is not the largest. These findings support the potential of the combined infusion as an experimental functional intervention for hyperlipidemia, but further research with a larger sample size, longer treatment duration, controlled feed intake, and additional biochemical markers is needed before clinical application can be considered.

REFERENCES

Cacciola, N. A., De Cicco, P., Milanović, M., Milovanović, I., Mišan, A., Kojić, D., Simeunović, J., Blagojević, D., Popović, T., Arsić, A., Pilija, V., Mandić, A., Borrelli, F., & Milić, N. (2024). Role of Arthrospira platensis in preventing and treating high-fat diet-induced hypercholesterolemia in adult rats. *Nutrients*, *16*(12), 1827. https://doi.org/10.3390/nu16121827

Cacciola, N. A., De Cicco, P., Milanovic, M., Milovanovic, I., Misan, A., Kojic, D., Simeunovic, J., Blagojevic, D., Popovic, T., & Milic, N. (2024). Role of Arthrospira platensis in Preventing and Treating High-Fat Diet-Induced Hypercholesterolemia in Adult Rats. *Nutrients*, *16*(12), 1827. https://doi.org/10.3390/nu16121827

Deng, R., & Chow, T. J. (2010). Hypolipidemic, antioxidant, and antiinflammatory activities of microalgae Spirulina. *Cardiovascular Therapeutics*, *28*(4), e33–e45. https://doi.org/10.1111/j.1755-5922.2010.00200.x

Ezeh, K. J., & Ezeudemba, O. (2021). Hyperlipidemia: A review of the novel methods for the management of lipids. *Cureus*, *13*(7), e16412. https://doi.org/10.7759/cureus.16412

Ference, B. A., Ginsberg, H. N., Graham, I., Ray, K. K., Packard, C. J., Bruckert, E., Hegele, R. A., Krauss, R. M., Raal, F. J., Schunkert, H., Watts, G. F., Borén, J., Fazio, S., Horton, J. D., Masana, L., Nicholls, S. J., Nordestgaard, B. G., van de Sluis, B., Taskinen, M. R., & Catapano, A. L. (2017). Low-density lipoproteins cause atherosclerotic cardiovascular disease: Evidence from genetic, epidemiologic, and clinical studies. *European Heart Journal*, *38*(32), 2459–2472. https://doi.org/10.1093/eurheartj/ehx144

Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*, *18*(6), 499–502. https://doi.org/10.1093/clinchem/18.6.499

Hermawan, A. (2024). Mengintip celah antara potensi dan tantangan big data pada layanan jaminan sosial ketenagakerjaan Indonesia. *Jurnal Jamsostek*, *2*(2), 185–206. https://doi.org/10.61626/jamsostek.v2i2.59

Hernawati, & others. (2018). The Role of Red Dragon Fruit Peel (Hylocereus polyrhizus) to Improvement Blood Lipid Levels of Hyperlipidaemia Male Mice. *Journal of Physics: Conference Series*, *1013*, 12167. https://doi.org/10.1088/1742-6596/1013/1/012167

Huang, H., Liao, D., Pu, R., & Cui, Y. (2018). Quantifying the effects of spirulina supplementation on plasma lipid and glucose concentrations, body weight, and blood pressure. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, *11*, 729–742. https://doi.org/10.2147/DMSO.S185672

Jang, H. H., Hwang, Y. J., & Lee, S. H. (2023). Effects of anthocyanin supplementation on blood lipid levels: A systematic review and meta-analysis. *Frontiers in Nutrition*, *10*, 1207751. https://doi.org/10.3389/fnut.2023.1207751

Mach, F., Baigent, C., Catapano, A. L., Koskinas, K. C., Casula, M., Badimon, L., Chapman, M. J., De Backer, G. G., Delgado, V., Ference, B. A., Graham, I., Halliday, A., Landmesser, U., Mihaylova, B., Pedersen, T. R., Riccardi, G., Richter, D. J., Sabatine, M.

S., Taskinen, M. R., & Wiklund, O. (2020). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. *European Heart Journal*, *41*(1), 111–188. https://doi.org/10.1093/eurheartj/ehz455

Nurliyana, R., Syed Zahir, I., Mustapha Suleiman, K., Aisyah, M. R., & Kamarul Rahim, K. (2010). Antioxidant study of pulps and peels of dragon fruits: A comparative study. *International Food Research Journal*, *17*(2), 367–375.

Panjaitan, R. G. P., & Amelia, S. (2022). Antihypercholesterolemic power of red dragon fruit (Hylocereus polyrhizus) peel extract. *Pharmacognosy Journal*, *14*(3), 518–523. https://doi.org/10.5530/pj.2022.14.83

Putriningtyas, N. D., Permatasari, I., Oktaviani, D., Raha, A. S., & Wahyuningsih, S. (2020). Red dragon fruit (Hylocereus spp.) peel marmalade effectively improve blood glucose and lipid profile of hypercholesterolemic Wistar rats. *Jurnal Gizi Indonesia (The Indonesian Journal of Nutrition)*, *9*(1), 61–67. https://doi.org/10.14710/jgi.9.1.61-67

Qin, Y., Xia, M., Ma, J., Hao, Y. T., Liu, J., Mou, H. Y., Cao, L., & Ling, W. H. (2009). Anthocyanin supplementation improves serum LDL- and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects. *The American Journal of Clinical Nutrition*, *90*(3), 485–492. https://doi.org/10.3945/ajcn.2009.27814

Rader, D. J., & Hovingh, G. K. (2014). HDL and cardiovascular disease. *The Lancet*, *384*(9943), 618–625. https://doi.org/10.1016/S0140-6736(14)61217-4

Serban, M. C., Sahebkar, A., Dragan, S., Stoichescu-Hogea, G., Ursoniu, S., Andrica, F., & Banach, M. (2016). A systematic review and meta-analysis of the impact of Spirulina supplementation on plasma lipid concentrations. *Clinical Nutrition*, *35*(4), 842–851. https://doi.org/10.1016/j.clnu.2015.09.007

Von Eckardstein, A., Nordestgaard, B. G., Remaley, A. T., & Catapano, A. L. (2023). High-density lipoprotein revisited: Biological functions and clinical relevance. *European Heart Journal*, *44*(16), 1394–1407. https://doi.org/10.1093/eurheartj/ehac605

Wybraniec, S., & Mizrahi, Y. (2002). Fruit flesh betacyanin pigments in Hylocereus cacti. *Journal of Agricultural and Food Chemistry*, *50*(21), 6086–6089. https://doi.org/10.1021/jf020145k